cifically binds to, or is complementary to an RNA that is encoded in a genome (e.g., a human genome), in which the distance in the genome between the 5' end of the coding region of the RNA and the 3' end of the coding region of the RNA is less than 1 kb, less than 2 kb, less than 3 kb, less than 4 kb, less than 5 kb, less than 7 kb, less than 8 kb, less than 9 kb, less than 10 kb, or less than 20 kb.

[0064] It is to be understood that any oligonucleotide provided herein can be excluded. In some embodiments, a single stranded oligonucleotide is not complementary to SEQ ID NO: 497807.

[0065] In some embodiments, a single-stranded oligonucleotide is complementary to a sequence within nucleotides 1 to 2897 or 2931 to 4046 of SEQ ID NO: 272. In some embodiments, a single-stranded oligonucleotide is complementary to a sequence within nucleotides 1 to 2737 or 3137 to 4024 of SEQ ID NO: 399.

[0066] In some embodiments, it has been found that single stranded oligonucleotides disclosed herein may increase expression of mRNA corresponding to the gene by at least about 50% (i.e. 150% of normal or 1.5 fold), or by about 2 fold to about 5 fold. In some embodiments, expression may be increased by at least about 15 fold, 20 fold, 30 fold, 40 fold, 50 fold or 100 fold, or any range between any of the foregoing numbers. It has also been found that increased mRNA expression has been shown to correlate to increased protein expression.

[0067] In some or any of the embodiments of the oligonucleotides described herein, or processes for designing or synthesizing them, the oligonucleotides will upregulate gene expression and may specifically bind or specifically hybridize or be complementary to the PRC2 binding RNA that is transcribed from the same strand as a protein coding reference gene. The oligonucleotide may bind to a region of the PRC2 binding RNA that originates within or overlaps an intron, exon, intron exon junction, 5' UTR, 3' UTR, a translation initiation region, or a translation termination region of a protein coding sense strand of a reference gene (refGene).

[0068] In some or any of the embodiments of oligonucleotides described herein, or processes for designing or synthesizing them, the oligonucleotides will upregulate gene expression and may specifically bind or specifically hybridize or be complementary to a PRC2 binding RNA that transcribed from the opposite strand (the antisense strand) of a protein coding reference gene. The oligonucleotide may bind to a region of the PRC2 binding RNA that originates within or overlaps an intron, exon, intron exon junction, 5' UTR, 3' UTR, a translation initiation region, or a translation termination region of a protein coding antisense strand of a reference gene

[0069] The oligonucleotides described herein may be modified, e.g., comprise a modified sugar moiety, a modified internucleoside linkage, a modified nucleotide and/or combinations thereof. In addition, the oligonucleotides can exhibit one or more of the following properties: do not induce substantial cleavage or degradation of the target RNA; do not cause substantially complete cleavage or degradation of the target RNA; do not activate the RNAse H pathway; do not activate RISC; do not recruit any Argonaute family protein; are not cleaved by Dicer; do not mediate alternative splicing; are not immune stimulatory; are nuclease resistant; have improved cell uptake compared to unmodified oligonucleotides; are not toxic to cells or mammals; may have improved endosomal exit; do interfere with interaction of lncRNA with PRC2, preferably the Ezh2 subunit but optionally the Suz12, Eed, RbAp46/48 subunits or accessory factors such as Jarid2; do decrease histone H3 lysine-27 methylation and/or do upregulate gene expression.

[0070] Oligonucleotides that are designed to interact with RNA to modulate gene expression are a distinct subset of base sequences from those that are designed to bind a DNA target (e.g., are complementary to the underlying genomic DNA sequence from which the RNA is transcribed).

[0071] Any of the oligonucleotides disclosed herein may be linked to one or more other oligonucleotides disclosed herein by a linker, e.g., a cleavable linker.

Method for Selecting Candidate Oligonucleotides for Activating Expression of UTRN

[0072] Methods are provided herein for selecting a candidate oligonucleotide for activating or enhancing expression of UTRN. The target selection methods may generally involve steps for selecting single stranded oligonucleotides having any of the structural and functional characteristics disclosed herein. Typically, the methods involve one or more steps aimed at identifying oligonucleotides that target a PRC2-associated region that is functionally related to UTRN, for example a PRC2-associated region of a lncRNA that regulates expression of UTRN by facilitating (e.g., in a cis-regulatory manner) the recruitment of PRC2 to the UTRN gene. Such oligonucleotides are expected to be candidates for activating expression of UTRN because of their ability to hybridize with the PRC2-associated region of a nucleic acid (e.g., a lncRNA). In some embodiments, this hybridization event is understood to disrupt interaction of PRC2 with the nucleic acid (e.g., a lncRNA) and as a result disrupt recruitment of PRC2 and its associated co-repressors (e.g., chromatin remodeling factors) to the UTRN gene locus.

[0073] Methods of selecting a candidate oligonucleotide may involve selecting a PRC2-associated region (e.g., a nucleotide sequence as set forth in any one of SEQ ID NOS: 5 to 462) that maps to a chromosomal position encompassing or in proximity to the UTRN gene (e.g., a chromosomal position having a sequence as set forth in any one of SEQ ID NOS: 1 to 4). The PRC2-associated region may map to the strand of the chromosome comprising the sense strand of the UTRN gene, in which case the candidate oligonucleotide is complementary to the sense strand of the UTRN gene (i.e., is antisense to the UTRN gene). Alternatively, the PRC2-associated region may map to the strand of the first chromosome comprising the antisense strand of the UTRN gene, in which case the oligonucleotide is complementary to the antisense strand (the template strand) of the UTRN gene (i.e., is sense to the UTRN gene).

[0074] Methods for selecting a set of candidate oligonucleotides that is enriched in oligonucleotides that activate expression of UTRN may involve selecting one or more PRC2-associated regions that map to a chromosomal position that encompasses or that is in proximity to the UTRN gene and selecting a set of oligonucleotides, in which each oligonucleotide in the set comprises a nucleotide sequence that is complementary with the one or more PRC2-associated regions. As used herein, the phrase, "a set of oligonucleotides that is enriched in oligonucleotides that activate expression of" refers to a set of oligonucleotides that has a greater number of oligonucleotides that activate expression of a target gene (e.g., UTRN) compared with a random selection of